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Production of glycoproteins in transgenic animals has some of the same problems as mammalian cell culture. While the "production" of a glycoprotein is inherently better controlled, it is also less susceptible to manipulation. If glycosylation is not complete, there is little that can be done with the animals to alter the outcome. With transgenic animals there is often another problem. While the predominant sialic acid in humans is N-acetyl-neuraminic acid (NeuAc), goats, sheep and cows all produce a large fraction of their total sialic acid as N-glycolyl-neuraminic acid (NeuGc). Although the impact of this modification is not yet fully explored from a functional or regulatory perspective, it is known that the NeuGc substitution is antigenic in humans (Varki (1992) *Glycobiology* 2: 25-40).

Please rewrite the paragraph at page 3, line 5 as follows:

Sialyltransferases that are useful in the methods of the invention typically have a sialyl motif that comprises about 48-50 amino acids, within which about 40% of the amino acids are identical to the consensus sequence RCAVVSSAG---DVGSKT (where --- indicates a variable number of amino acid residues such that the motif is about 48-50 residues in length). Examples of sialyltransferases that are suitable for use in the present invention include ST3Gal III (preferably a rat ST3Gal III), ST3Gal IV, ST3Gal I, ST6Gal I, ST3Gal V, ST6Gal II, ST6GalNAc II, and ST6GalNAc III (the sialyltransferase non-enclature used herein is as described in Tsuji *et al.* (1996) *Glycobiology* 6: v-xiv). The methods of the invention can involve sialylation of recombinant glycoproteins with more than one sialyltransferase; for example, with an ST3Gal III and an ST3Gal I, or an ST3 Gal III and an ST6 Gall, or other combinations of enzymes. The sialic acid donor moiety used in the claimed methods is generally CMP-sialic acid, which can be added to the reaction directly or can be enzymatically generated *in situ*. The sialic acids used in a preferred embodiment are selected from the group consisting of NeuAc and NeuGc.

Please rewrite the paragraph at page 4, line 1 as follows:

B4

Ara

= arabinosyl;

B

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Fru = fructosyl; Fuc = fucosyl;

Gal = galactosyl;

GalNAc = N-acetylgalactosaminyl;

Glc = glucosyl;

GlcNAc = N-acetylglucosaminyl;

Man = mannosyl; and

NeuAc = sialyl (typically N-acetylneuraminyl).

IN THE CLAIMS:

Please amend claims 12, 23, 44, 57 and 82 as follows:

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12. (Amended) A commercial-scale method of sialylating a saccharide

group on a recombinant glycoprotein, the method comprising contacting a saccharide

group which comprises a galactose or N-acetylgalactosarnine acceptor moiety on a

recombinant glycoprotein with a sialic acid donor moiety and a recombinant bacterial

sialyltransferase in a reaction mixture which provides reactants required for

6 sialyltransferase activity for a sufficient time and under appropriate conditions to transfer

sialic acid from said sialic acid donor molety to said saccharide group.

Rb

- 23. (Amended) A commercial-scale method of sialylating a saccharide
- 2 group on a recombinant glycoprotein, the method comprising contacting a saccharide
- 3 group which comprises a galactose or an N-acetylgalactosamine acceptor moiety on a
- 4 recombinant glycoprotein with a sialic acid donor moiety and a bacterial sialyltransferase
- 5 in a reaction mixture which provides reactants required for sialyltransferase activity for a
- 6 sufficient time and under appropriate conditions to transfer sialic acid from said sialic
- 7 _acid donor moiety to said saccharide.

B7

44. (Amended) A commercial-scale method for in vitro sialylation of

saccharide groups on a glycoprotein, said method comprising contacting said saccharide

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3 groups with a sialyltransferase, wherein the sialyltransferase is a bacterial

- sialyltransferase, a sialic acid donor moiety, and other reactants required for
- sialyltransferase activity for a sufficient time and under appropriate conditions to transfer
- sialic acid from said sialic acid donor moiety to said saccharide group.

B8

57. (Amended) A commercial-scale method for in vitro sialylation of

8 terminal galactose residues on a glycoprotein, said method comprising contacting said

- glycoprotein with a reaction mixture that comprises a sialyltransferase, a sialic acid donor
- moiety, and other reactants required for sialyltransferase activity, for a sufficient time and
- under appropriate conditions to transfer sialic/acid from said sialic acid donor moiety to
- said terminal galactose residues.

B9

82. (Amended) A commercial-scale method for altering the

- glycosylation pattern of a glycoprotein in vitro, the method comprising contacting a
- 3 glycoprotein-linked saccharide with a galactosyltransferase in the presence of UDP-
- 4 galactose under suitable conditions for the galactosyltransferase to transfer a galactose
- 5 residue from the UDP-galactose to the saccharide to form a galactosylated saccharide.

Please add the following new claims 98-102:



--98. (New) The method of claim 12, wherein the glycoprotein comprises

an immunoglobuljn.

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1

2

/99. (New) The method of claim 23, wherein the glycoprotein comprises an

immunoglobulin.

 $\mathcal{B}_{|_{\mathcal{G}}}$

100. (New) The method of claim 44, wherein the glycoprotein comprises

2 an immunoglobulin.

l

101. (New) The method of claim 57, wherein the glycoprotein comprises

2 an immunoglobulin.